


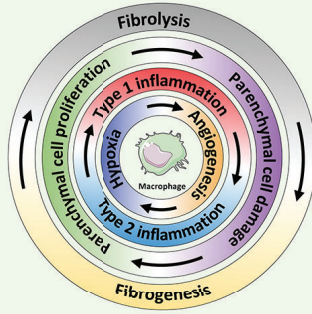

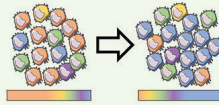


HEPATOLOGY COMMUNICATIONS

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OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION
FOR THE STUDY OF LIVER DISEASES

	Old dogmas	New insights
Cell identification	<p>« Kupffer cells » (e.g. F4/80⁺ cells)</p>  <p>No distinction between myeloid cell types and functions</p>	<p>Monocyte-derived liver macrophages (MoMFs) Origin: bone-marrow</p> <p>Kupffer cells (KCs) Origin: yolk sac</p>  <p>Increasing knowledge on distinct:</p> <ul style="list-style-type: none"> • Ontogeny • Location and migratory properties • Plasticity • Subpopulations • Functions in health and disease
Polarization	<p>M1 or M2 macrophages</p>  <p>Pro-inflammatory Anti-fibrogenic Anti-inflammatory Pro-fibrogenic</p> <p>Dichotomic view</p>	<p>Spectrum of activation states and functions</p> 
Therapeutic implications	<p>Immunodepleting approach</p>  <p>Loss or inhibition of phagocytes deemed beneficial</p>	<p>Immunomodulating approaches</p>  <p>Influence effective macrophage balance by:</p> <ul style="list-style-type: none"> • Targeted gene expression modulation • Chemokine receptor antagonism • Shaping activating signals • Subset-selective targeting by nanomedicine • Disease-stage specific interventions on macrophage functions

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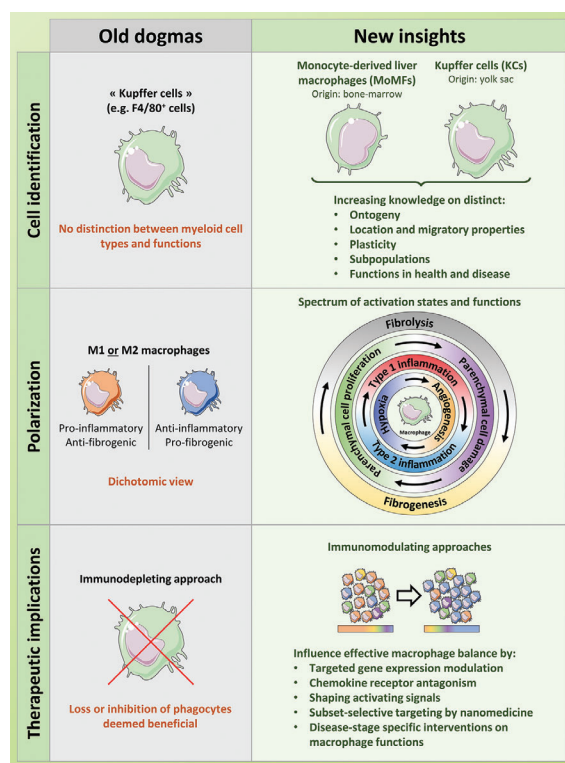
June 2019

Editorial

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Kouichi Miura and Hironori Yamamoto

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Cover Figure: Old dogmas versus new insights on liver macrophages. Liver macrophages have long been regarded as a homogeneous population and designated as F4/80+ KCs. Innovative new techniques, such as cell tracking, multi-omics phenotyping, and single-cell RNA sequencing, unraveled a previously unrecognized heterogeneity in liver macrophage origins and functions. The simplistic dichotomous view of M1-versus M2-polarized macrophages also appears outdated as macrophages of virtually all intermediate phenotypes have been described depending on the pathology or activating signals they are exposed to. Considering the multifaceted roles of liver macrophages in promoting or preventing tissue damage and repair, immunomodulating (e.g., gene expression modulation, chemokine receptor antagonism, à la carte activating signals) rather than immunodepleting approaches need to be considered.

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